Notice of Allowability	Application No.	Applicant(s)	
	09/632,722	HIMMELSPACH ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *10/15/04*.

2. ☒ The allowed claim(s) is/are *1,4,6,8,9,11-15,17,19-33 and 44-46*.

3. ☒ The drawings filed on *26 January 2004* are accepted by the Examiner.

4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☒ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date 10/02/03
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

1. An Examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

2. Authorization of this Examiner's amendment was given in a telephone interview with Mr. Scott Ausenhus on October 15, 2004.

3. The Specification has been amended as follows:

On page 1 line 1 insert the following paragraph:

This application claims priority under 35 U.S.C. 119(a-d) to Application No. A 1377/99, filed on August 10, 1999.

4. The Claims have been amended as follows:

Claim 1 (Currently Amended) A [factor] Factor X analog which contains ~~a modification~~ one or more modifications in ~~the region of amino acid residues Glu226 to Ile235 of SEQ ID NO:2, such that amino acids Glu226 to Arg234 and amino acid 235 of SEQ ID NO:2 have the sequence Glu226-R8-R7-R6-R5-R4-R3-R2-Arg234-R1, wherein~~ SEQ ID NO:2 selected from the group consisting of:

~~a) R1 is Ile, Val, or Ala;~~

~~b) R2 is Thr, Ser, or Asn;~~

~~c) R3 is Phe, Leu, Arg, or Ile;~~

~~d) R4 is Asp, Lys, Thr, or Glu;~~

~~e) R5 is Asn, Ser, Lys, Met, Thr, or Asp;~~

~~f) R6 is Phe, Thr, Ser, Pro, Leu, or Ile;~~

~~g) R7 is Ser, Gln, Ile, Thr, Asn, or Pro; and~~

~~h) R8 is Gln, Ser, His, Tyr, or Glu.~~

a) Ile235 is Val or Ala;

b) Thr233 is Ser or Asn;

c) Leu232 is Phe, Arg or Ile;

d) Asn231 is Asp, Lys, Thr, or Glu;

e) Asn230 is Ser, Lys, Met, Thr, or Asp;

f) Asp229 is Phe, Thr, Ser, Pro, Leu, or Ile;

g) Gly228 is Ser, Gln, Ile, Thr, Asn, or Pro; and

h) Arg227 is Gln, Ser, His, Tyr, or Glu.

Claims 2-3 (Canceled)

Claim 4 (Currently Amended). The [factor] Factor X analog of claim 1, wherein the amino acid sequence of residues 227-233 ~~(R8-R7-R6-R5-R4-R3-R2)~~ is Gln227-Ser228-Phe229-Asn230-Asp231-Phe232-Thr233 (SEQ ID NO:17).

Claim 5 (Canceled)

Claim 6 (Currently Amended) The [factor] Factor X analog of claim 1, wherein the amino acid sequence [from] of residues 227-233 ~~(R8-R7-R6-R5-R4-R3-R2)~~ is Ser227-Gln228-Thr229-Ser230-Lys231-Leu232-Thr233 (SEQ ID NO:18).

Claim 7 (Canceled)

Claim 8 (Currently Amended) The [factor] Factor X analog of claim 1, wherein the modification forms a processing site for [factor] Factor XIa or a derivative thereof.

Claim 9 (Currently Amended) ~~A factor X analog comprising a factor X sequence which contains (1) a modification in the region of amino acid residues Glu226 to Ile235 of SEQ ID NO:2, such that amino acids Glu226 to Arg234 and amino acid 235 of SEQ ID NO:2 have the sequence Glu226-R8-R7-R6-R5-R4-R3-R2-Arg234-R1, and (2) an additional modification in a C-terminal region of the factor X sequence, and wherein~~

~~a) R1 is Ile, Val, or Ala;~~

~~b) R2 is Thr, Ser, or Asn;~~

~~c) R3 is Phe, Leu, Arg, or Ile;~~

~~d) R4 is Asp, Lys, Thr, or Glu;~~

~~e) R5 is Asn, Ser, Lys, Met, Thr, or Asp;~~

~~f) R6 is Phe, Thr, Ser, Pro, Leu, or Ile;~~

~~g) R7 is Ser, Gln, Ile, Thr, Asn, or Pro;~~

~~h) R8 is Gln, Ser, His, Tyr, or Glu.~~

A Factor X analog which

(i) contains one or more modifications in SEQ ID NO:2 selected from the group consisting of:

a) Ile235 is Val or Ala;

b) Thr233 is Ser or Asn;

c) Leu232 is Phe, Arg or Ile;

d) Asn231 is Asp, Lys, Thr, or Glu;

e) Asn230 is Ser, Lys, Met, Thr, or Asp;

f) Asp229 is Phe, Thr, Ser, Pro, Leu, or Ile;

g) Gly228 is Ser, Gln, Ile, Thr, Asn, or Pro; and

h) Arg227 is Gln, Ser, His, Tyr, or Glu; and

(ii) has a further modification occurring at Lys370 and/or within a segment extending from Arg 469 to Ser476 of SEQ ID NO:2.

Claim 10 (Canceled)

Claim 11 (Currently Amended) The [factor] Factor X analog of claim 1, wherein said modification permits an *in vivo* activation of the [factor] Factor X analog into native [factor] Factor Xa or a [factor] Factor Xa analog.

Claim 12 (Currently Amended) The [factor] Factor X analog of claim 1, wherein said modification permits an *in vitro* activation of the [factor] Factor X analog into native [factor] Factor Xa or a [factor] Factor Xa analog.

Claim 13 (Currently Amended) The [factor] Factor X analog of claim 1 that contains an intact ß-peptide.

Claim 14 (Currently Amended) The [factor] Factor X analog of claim 1 which is in the form of a double-chain molecule.

Claim 15 (Currently Amended) The [factor] Factor X analog of claim 1 having a shortened C-terminal region, wherein the C-terminal region corresponds to amino acid residues 476-487.

Claim 16 (Canceled)

Claim 17 (Currently Amended) A preparation comprising the [factor] Factor X analog of claim 1 or a precursor protein thereof.

Claim 18 (Canceled)

Claim 19 (Currently Amended) The preparation of claim 17, wherein the modification forms a cleavage site for [factor] Factor XIa or a derivative thereof.

Claim 20 (Currently Amended) The preparation of claim 17, wherein the [factor] Factor X analog is a Factor Xα analog.

Claim 21 (Currently Amended) The preparation of claim 17, wherein the [factor] Factor X analog has a shortened C-terminal amino acid sequence, wherein the C-terminal region corresponds to amino acid residues 476-487.

Claim 22 (Currently Amended) The preparation of claim 17, wherein the [factor] Factor X analog is a double-chain molecule.

Claim 23 (Currently Amended) The preparation of claim 17, wherein the [factor] Factor X analog is a single-chain [factor] Factor X analog in enzymatically inactive form that is at least 80% pure; and

the preparation does not contain inactive proteolytic intermediates of [factor] Factor X/Xa analog.

Claim 24 (Currently Amended) The preparation of claim 17, wherein the [factor] Factor X analog is a single-chain molecule.

Claim 25 (Currently Amended) The preparation of claim 17, wherein the modification permits an *in vivo* activation of the [factor] Factor X analog into native [factor] Factor Xa or a [factor] Factor Xa analog.

Claim 26 (Currently Amended) The preparation of claim 17, wherein the modification permits an *in vitro* activation of the [factor] Factor X analog into native [factor] Factor Xa or into a [factor] Factor Xa analog.

Claim 27 (Previously Presented) The preparation of claim 17 that is formulated as a pharmaceutical preparation.

Claim 28 (Currently Amended) A method for obtaining a preparation comprising an activated [factor] Factor X analog, the method comprising:

(a) providing the [factor] Factor X analog of claim 1; and

(b) activating the [factor] Factor X analog to obtain the activated [factor] Factor X analog.

Claim 29 (Previously Presented) The method of claim 28, further comprising formulating the preparation with a physiologically acceptable matrix.

Claim 30 (Previously Presented) The method of claim 28, further comprising combining the preparation with a blood factor or an activated form of a blood factor as an additional component.

Claim 31 (Currently Amended) The method of claim 30, wherein the additional component comprises at least one component with [factor] Factor VIII inhibitory bypass activity.

Claim 32 (Previously Presented) The preparation of claim 17 that is formulated as a pharmaceutical compound and present as a multi-component preparation.

Claim 33 (Previously Presented) A method for preparing a pharmaceutical composition, comprising formulating the preparation of claim 17 as pharmaceutical composition.

Claims 34-43 (Canceled)

Claim 44 (New) The Factor X analog as set forth in claim 9, wherein the further modification is a substitution located at the β-peptide cleavage site located between Arg469 and Gly470 of SEQ ID NO:2.

Claim 45 (New) The Factor X analog as set forth in claim 9, wherein the further modification is selected from a mutation, a deletion and an insertion between amino acid positions Arg469 and Ser476 of SEQ ID NO:2.

Claim 46 (New) A Factor X analog which

(i) contains one or more modifications in SEQ ID NO:2 selected from the group consisting of:

a) Ile235 is Val or Ala;

b) Thr233 is Ser or Asn;

c) Leu232 is Phe, Arg or Ile;

d) Asn231 is Asp, Lys, Thr, or Glu;

e) Asn230 is Ser, Lys, Met, Thr, or Asp;

f) Asp229 is Phe, Thr, Ser, Pro, Leu, or Ile;

g) Gly228 is Ser, Gln, Ile, Thr, Asn, or Pro; and

h) Arg227 is Gln, Ser, His, Tyr, Glu; and

(ii) has a further modification which is a deletion of Factor X β-peptide (Gly470 to Lys488 of SEQ ID NO:2).

5. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance".

Conclusion

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday from 9:00 a.m. to 6:30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS

Patent Examiner 10/15/04

JON WEBER
SUPERVISORY PATENT EXAMINER